213.1143-CIP

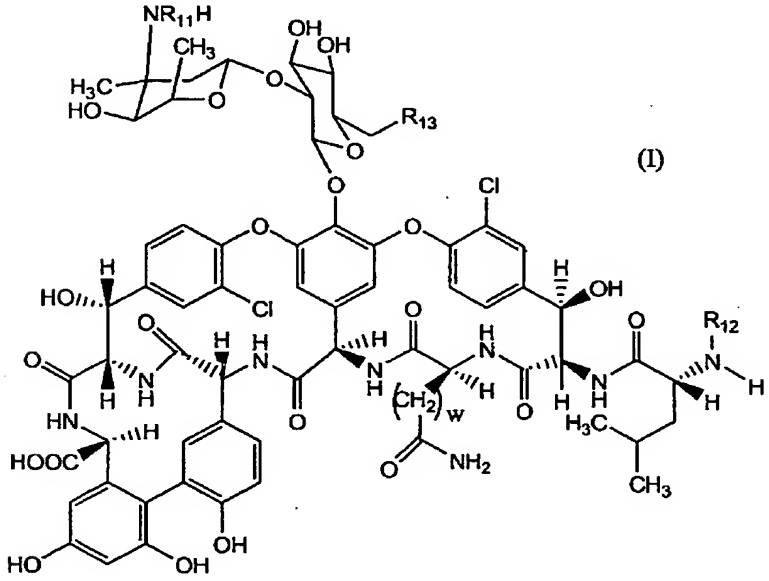
AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Original) A method of preparing a vancomycin-polymer conjugate, comprising:

reacting a vancomycin compound of the formula:



(I)

wherein

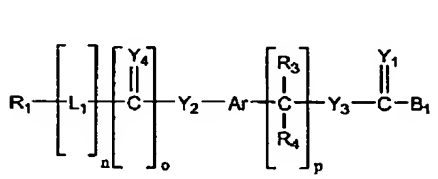
R_{11} and R_{12} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxyalkyl, phenoxyalkyl and C_{1-6} heteroalkoxys;

R_{13} is OH, NH-aryl, NH-aralkyl, or NH-C_{1-12} alkyl; and

w is 1 or 2;

with a polymer residue containing at least one leaving group capable of reacting with the sugar amino group of said vancomycin compound in the presence of at least about a ten-fold molar excess of triethylamine and a sufficient amount of dimethylformamide.

2. (Original) The method of claim 1, wherein said activated polymer residue is selected from the group consisting of:



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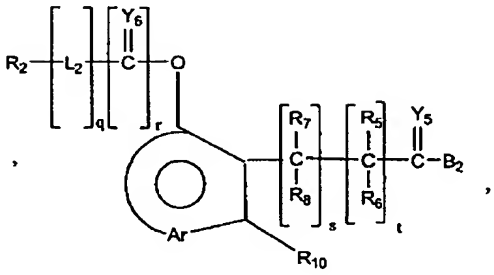

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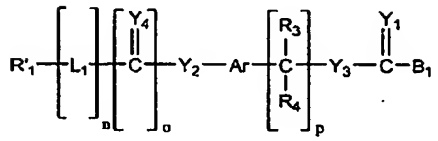

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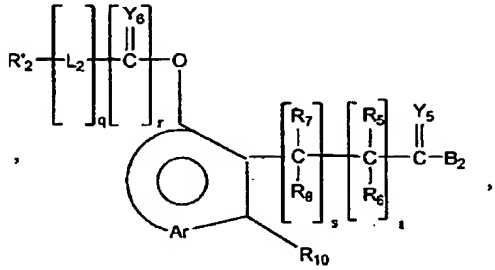

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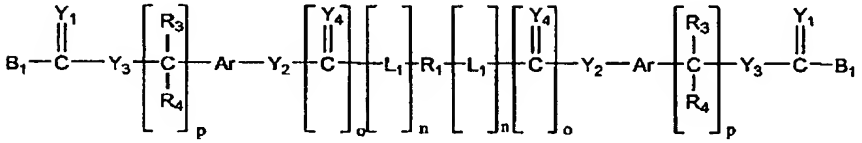

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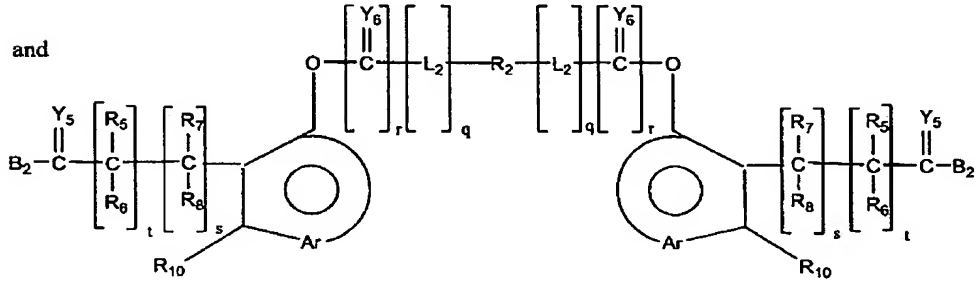


wherein:

R_1 and R_2 are independently selected polymer residues;

Y_{1-6} are independently selected from the group consisting of O, S or NR_9;

R_{3-10} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cyloalkyls, aryls,

substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxyalkyl, phenoxyalkyl and C_{1-6} hetero-alkoxys;

Ar is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

L_1 and L_2 are independently selected bifunctional linkers;

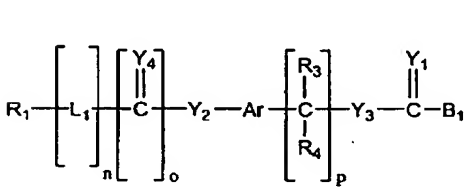
B_1 and B_2 are independently selected leaving groups;

p and t are independently selected positive integers;

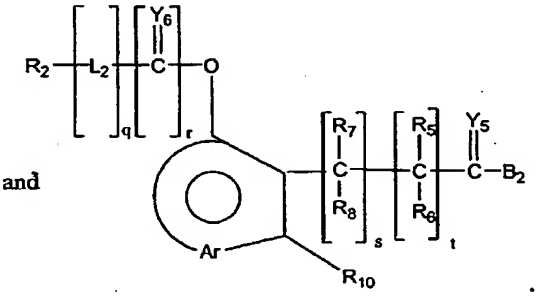
n, q and s are independently either zero or a positive integer; and

o and r are independently zero or one.

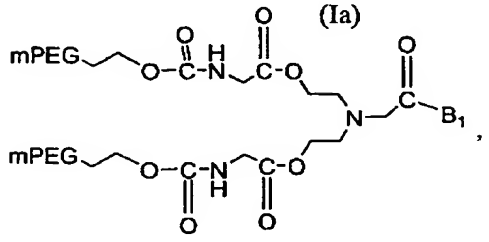
3. (Original) The method of claim 2, wherein said activated polymer residue is selected from the group consisting of



and



4. (Original) The method of claim 1, wherein said activated polymer residue is selected from the group consisting of:



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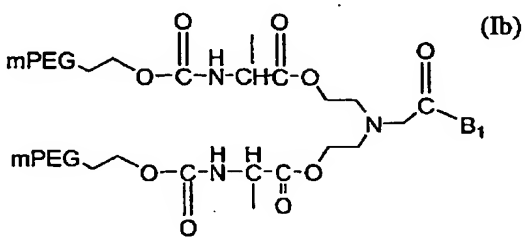
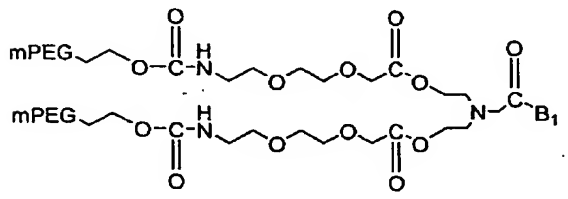
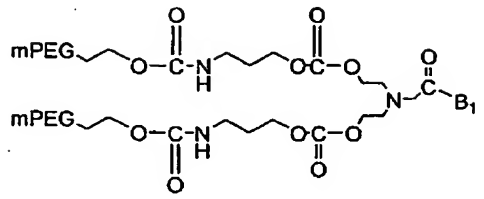


(Ib)



(Ic)



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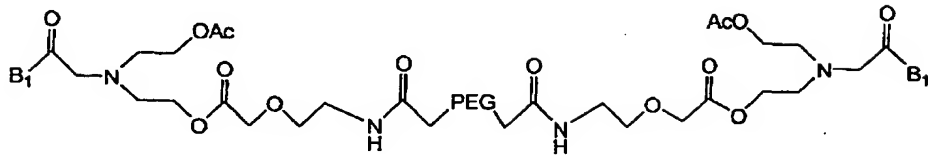

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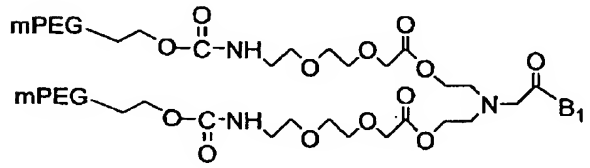

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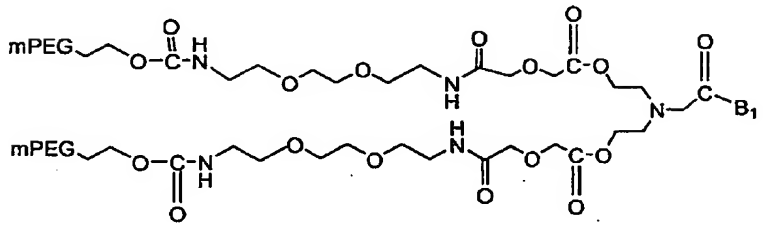
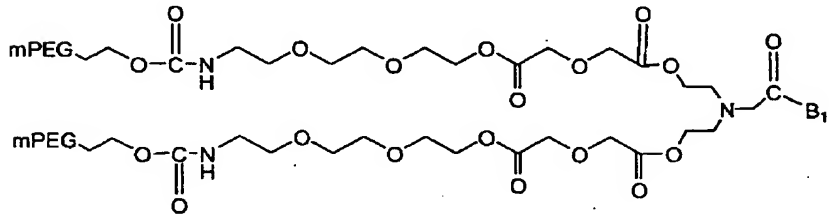
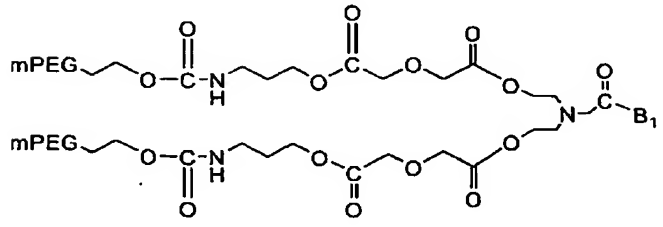


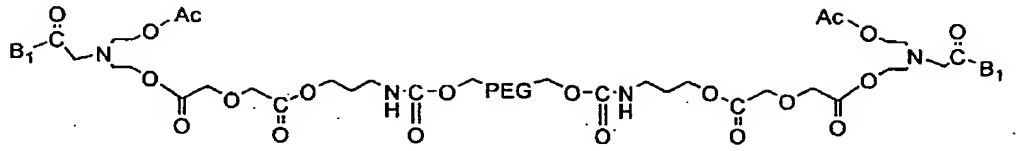
(Ig)



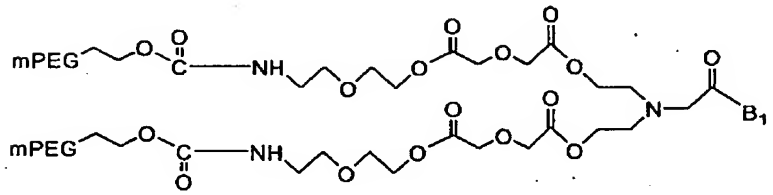
(Ih)



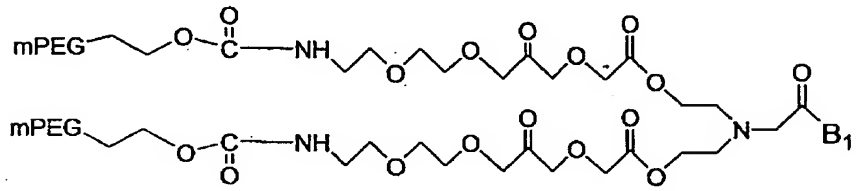
(Ii)



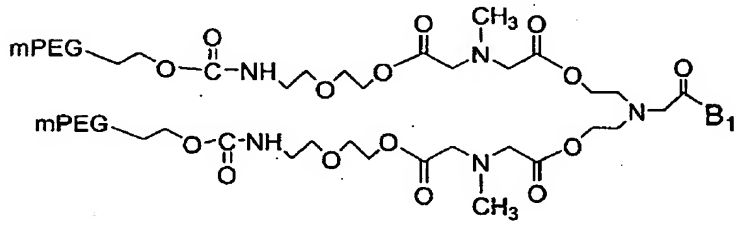
(Ij)



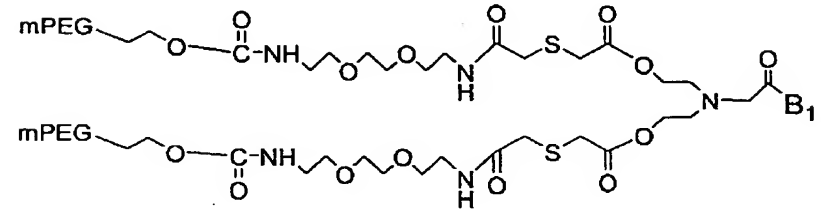
(Ik)



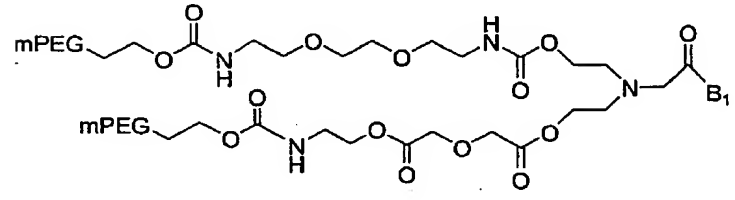
(Il)



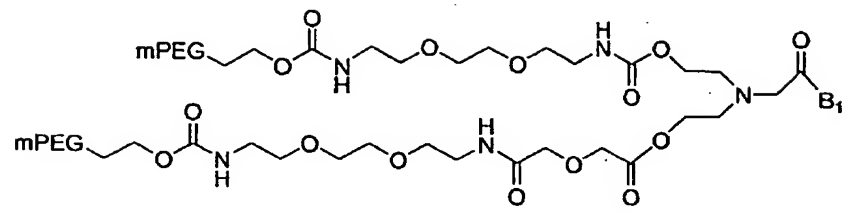
(Im)



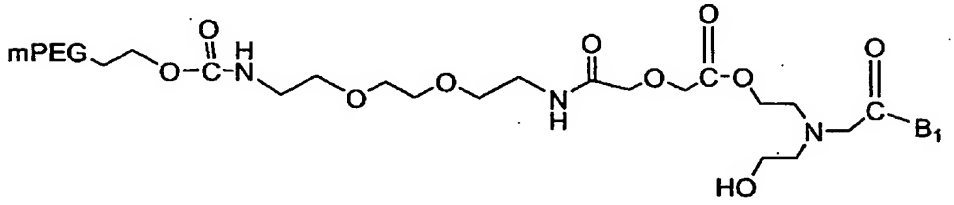
(In)



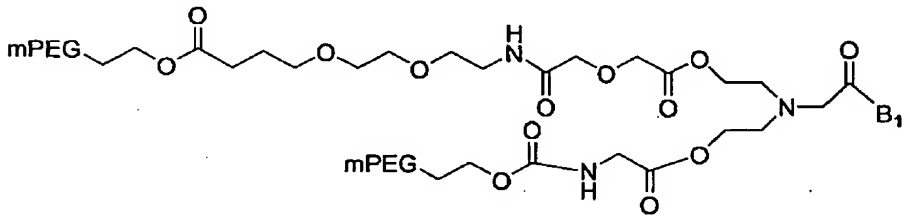
(Io)



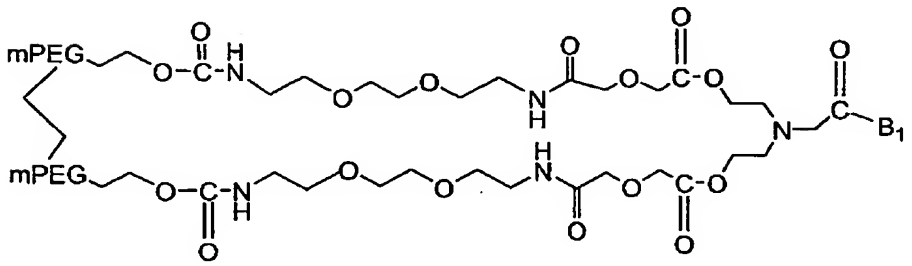
(Ip)



(Iq)

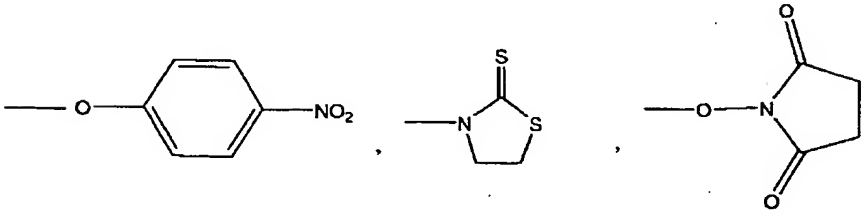


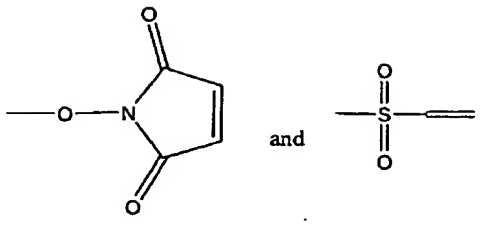
(Ir)



(Is)

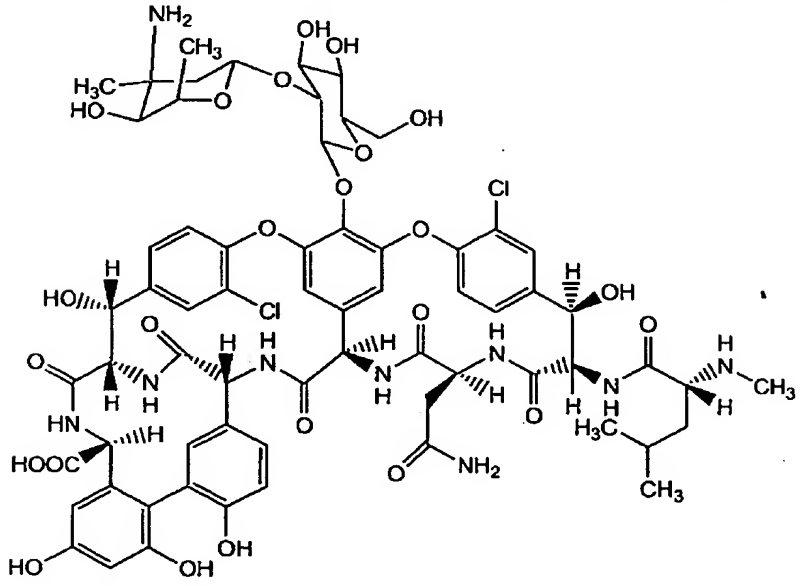
wherein B_1 is selected from the group consisting of:



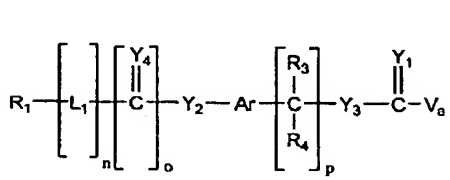


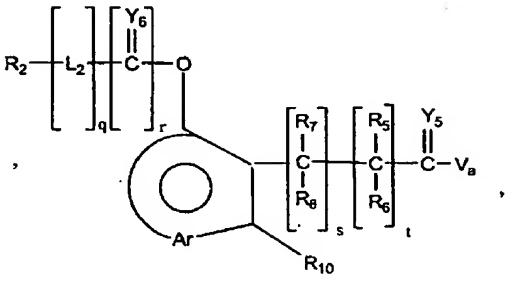
and

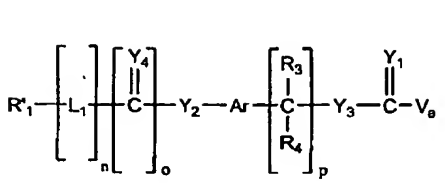
5. (Original) The method of claim 1, wherein said vancomycin compound is:

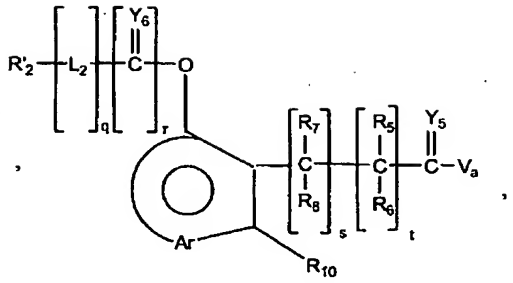


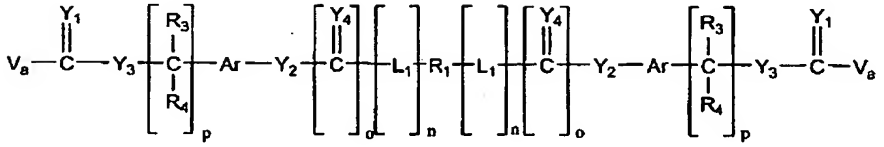
6. (Original) The method of claim 2, wherein said vancomycin polymer conjugate is selected from the group consisting of











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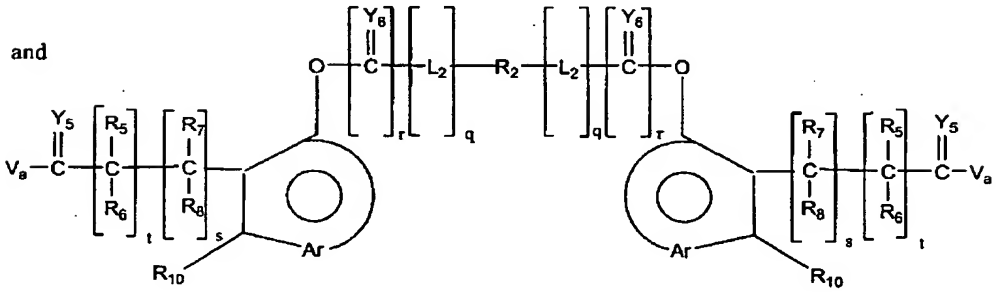

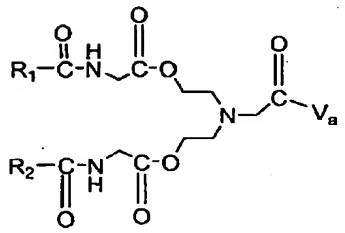

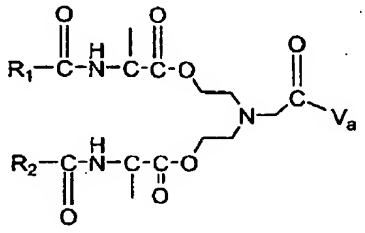

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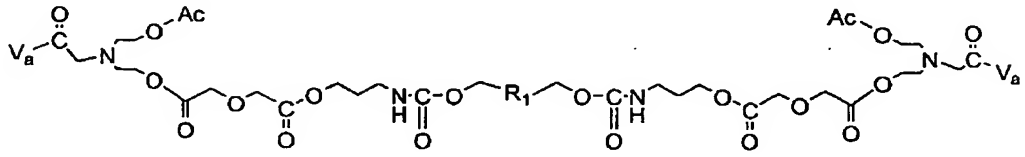
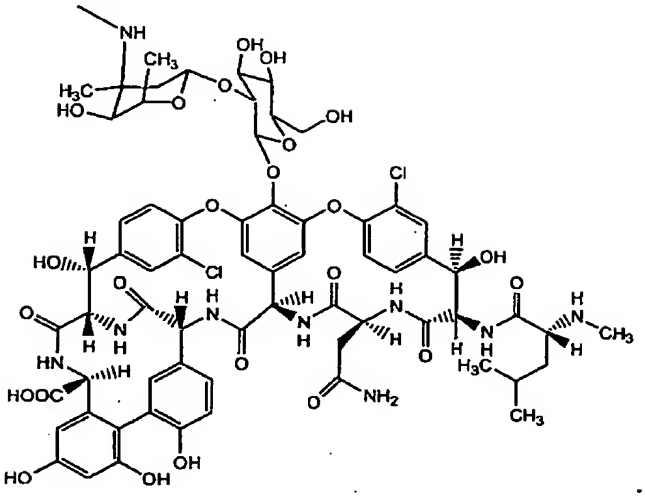
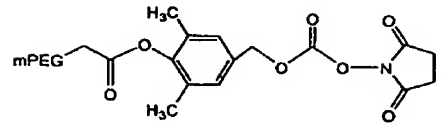
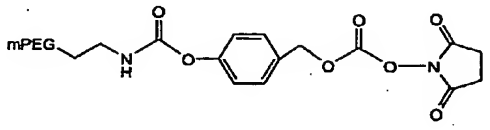


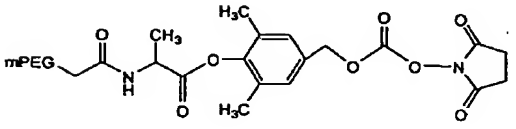
wherein V_a is

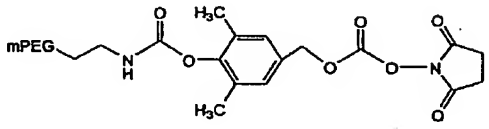


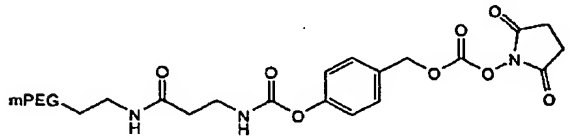
7. (Original) The method of claim 1, wherein said polymer containing said leaving group is selected from the group consisting of

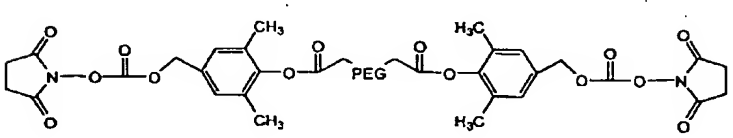


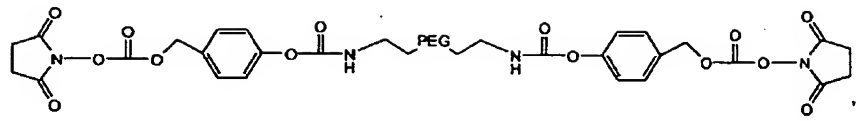


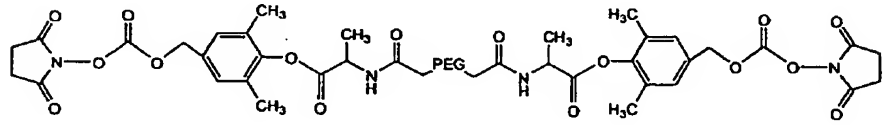


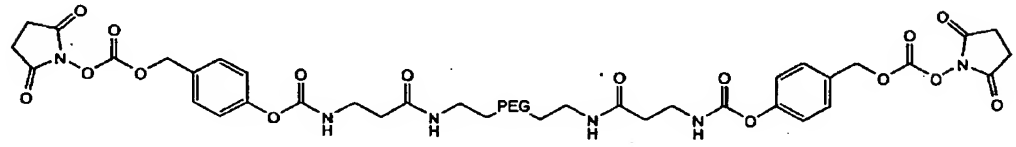


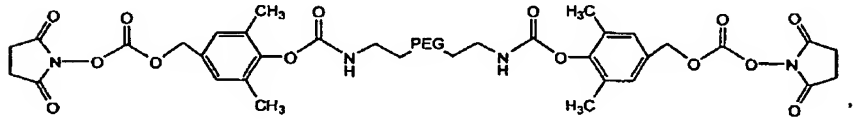


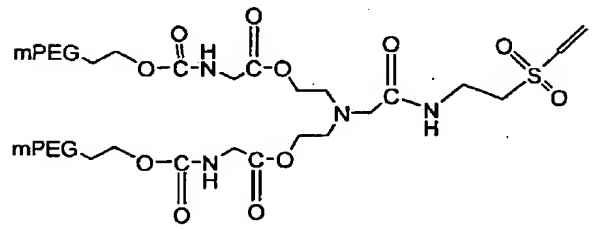












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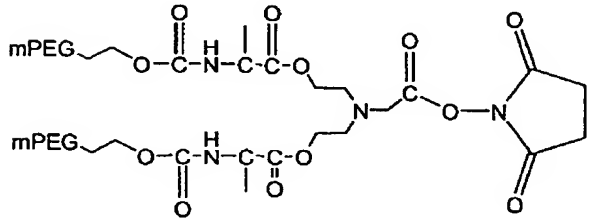
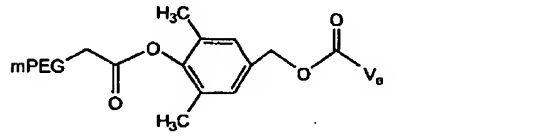
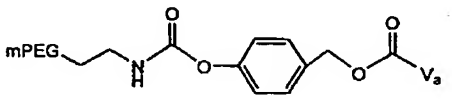


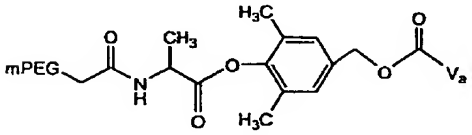
8. (Original) The method of claim 2, wherein R_1 and R_2 are independently selected polyalkylene oxide residues and R'_1 and R'_2 are independently selected branched polyalkylene oxide residues.

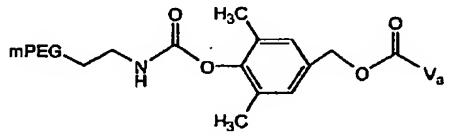
9. (Original) The method of claim 2, wherein R_1 and R_2 are independently selected polyethylene glycol residues and R'_1 and R'_2 are independently selected branched polyethylene glycol residues.

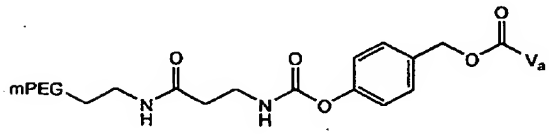
10. (Original) The method of claim 1, wherein said vancomycin-polymer conjugate is selected from the group consisting of

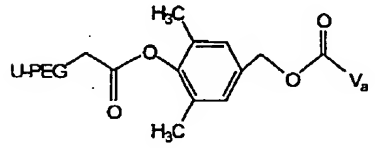


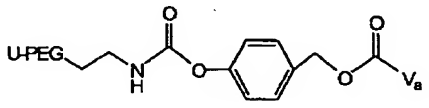


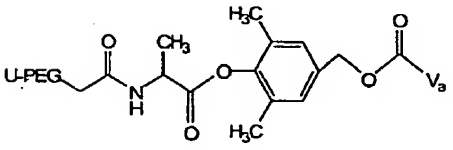


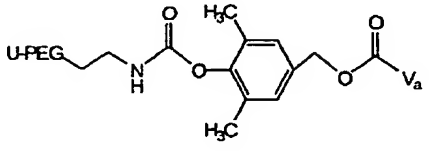


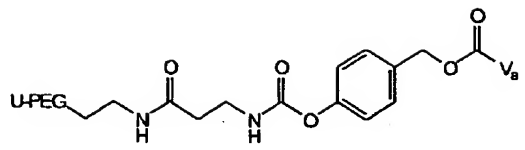


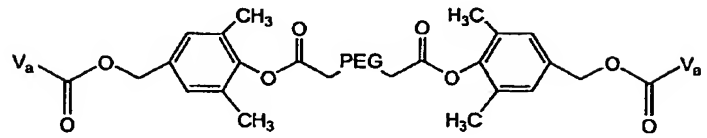


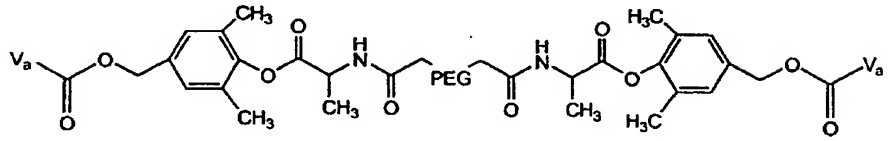


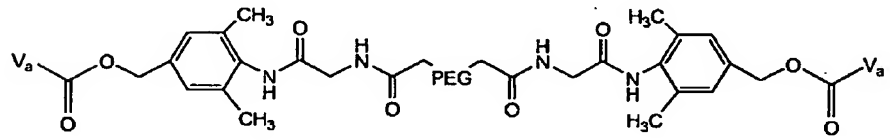


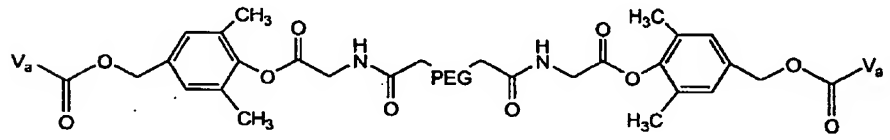


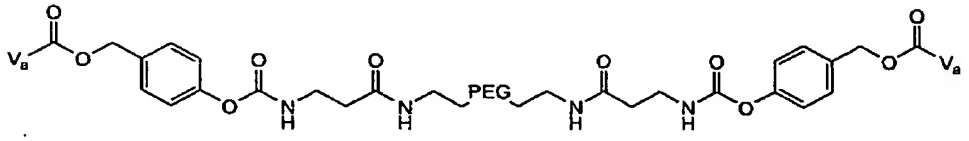


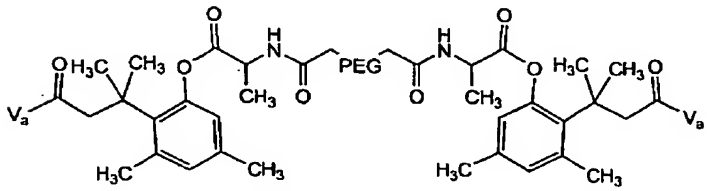


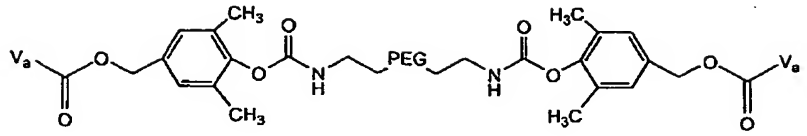


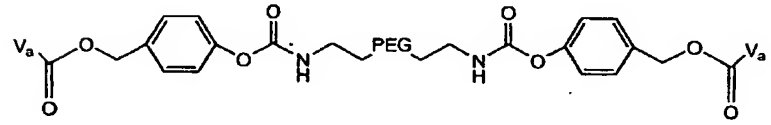


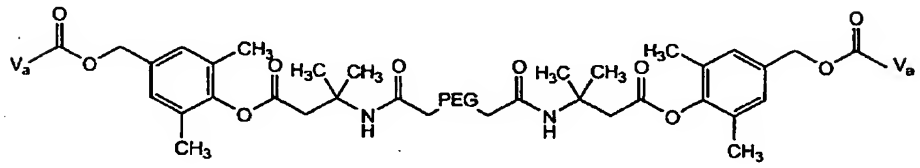


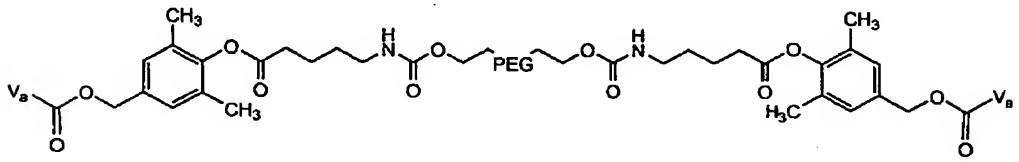


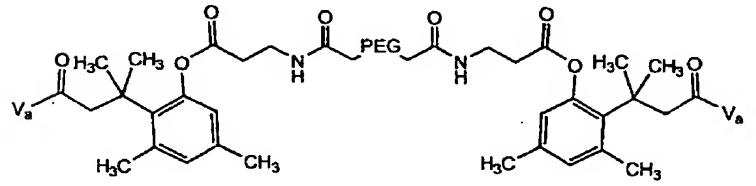


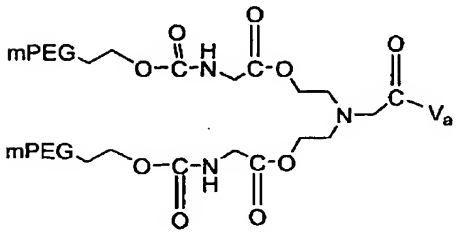


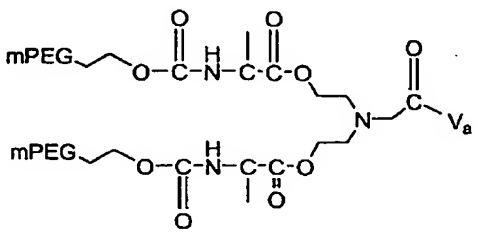












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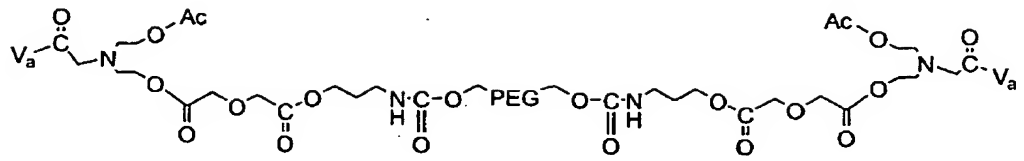


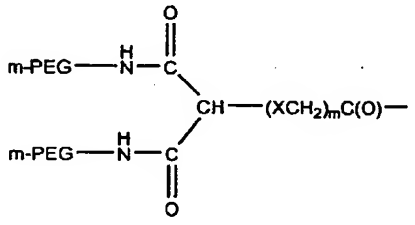
wherein

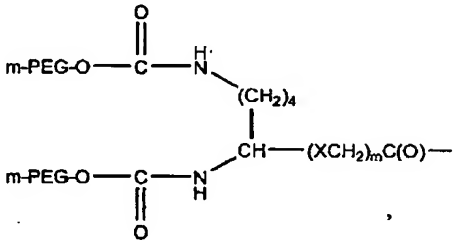
PEG is $-O(-CH_2CH_2O)_x-$;

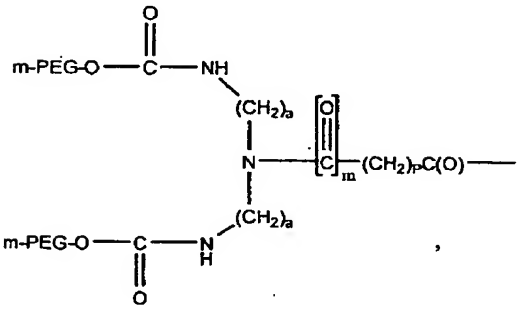
mPEG is $H_3CO(-CH_2CH_2O)_x-$;

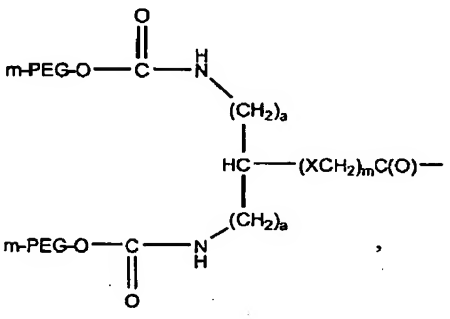
x is a positive integer selected from about 10 to about 2300, and

U-PEG is selected from the group consisting of

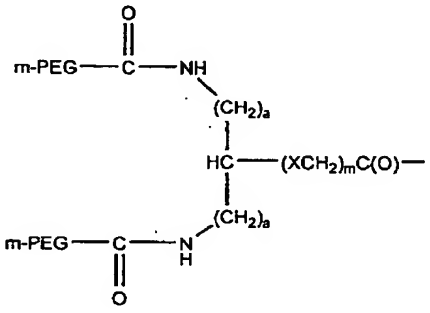




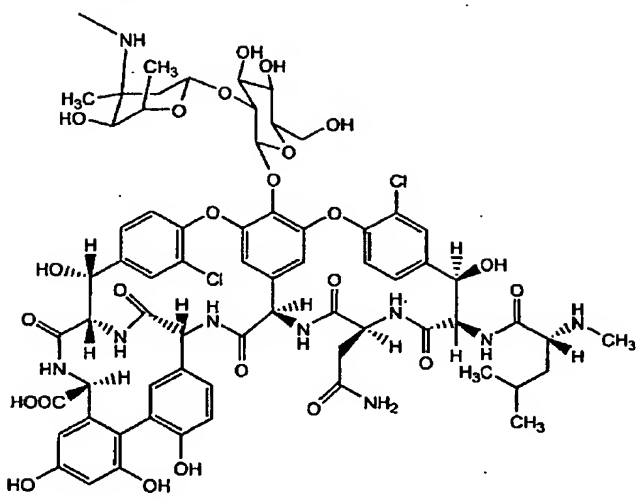




and

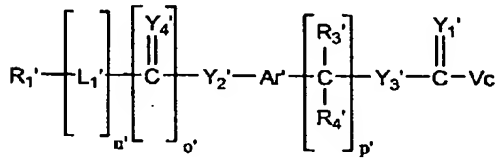


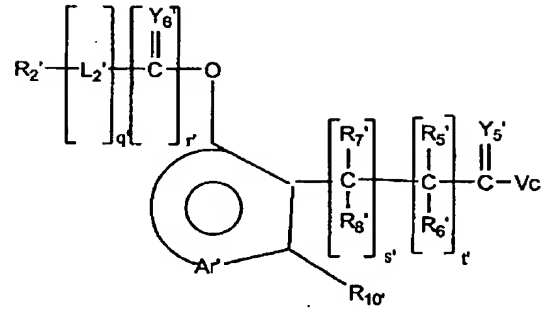
V_a is

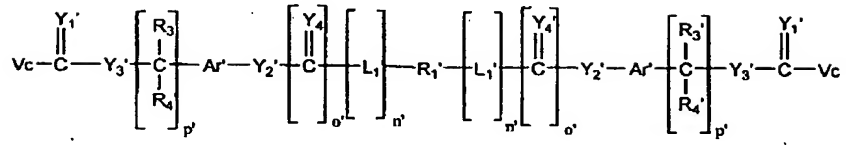


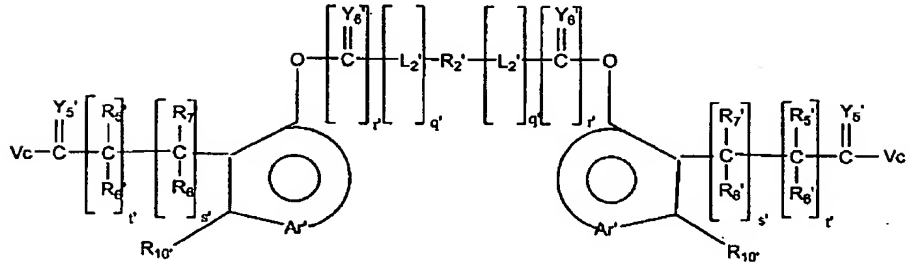
11. (Original) The method of claim 3, wherein R_1 and R_2 further comprise a capping group and said method further comprises reacting the vancomycin-polymer conjugate with a polymer residue containing at least one leaving group capable of reacting with the N-methyl amino group of said vancomycin compound in the presence of about a five-fold molar molar excess of dimethylaminopyridine (DMAP) and a sufficient amount of a solvent mixture comprising dichloromethane (DCM) and dimethyl formamide (DMF), whereby a vancomycin-polymer conjugate is formed in which a polymer residue is attached on both the sugar amino and the N-methyl amino of said vancomycin compound.

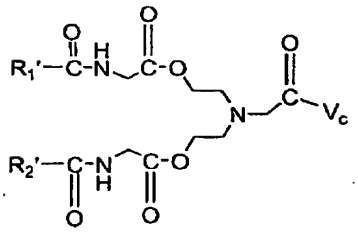
12. (Original) The method of claim 10, wherein said vancomycin-polymer conjugate containing said polymer residue attached on both of said sugar amino group and said N-methyl amino group is selected from the group consisting of:

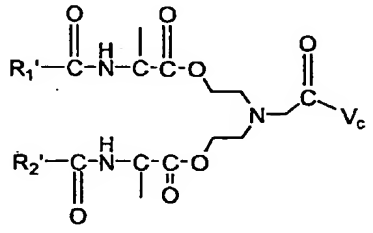




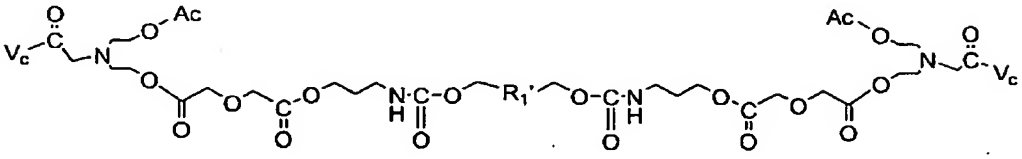






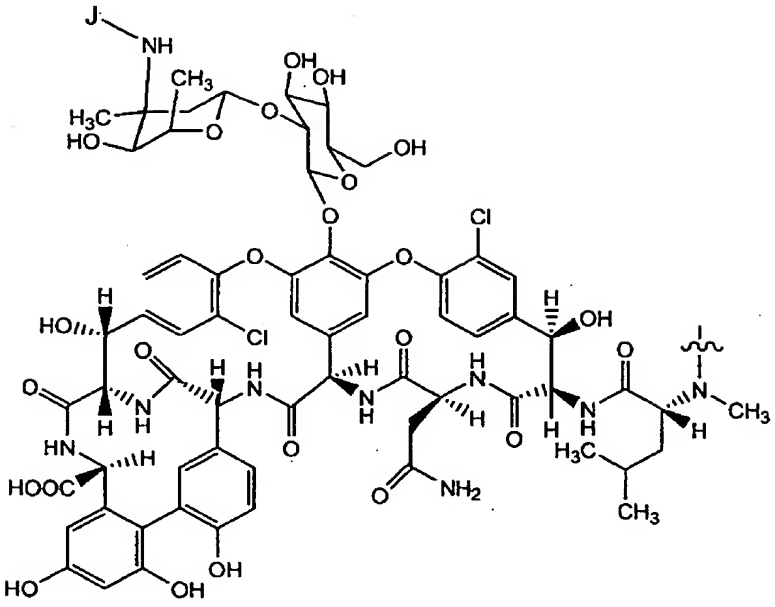


and



wherein

Vc is:



wherein:

J is H or a polymer residue containing a capping group,

R_1' and R_2' are independently selected polymeric residues;

Y_{1-6}' are independently selected from the group consisting of O, S or NR_9';

R_{3-10}' are the same or different and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxys, phenoxys and C_{1-6} heteroalkoxys;

Ar' is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

L_1' and L_2' are independently selected bifunctional linkers;

p' and t' are independently selected positive integers;

n', q' and s' are independently either zero or a positive integer;

o' and r' are independently zero or one; and

all other variables are as previously defined.

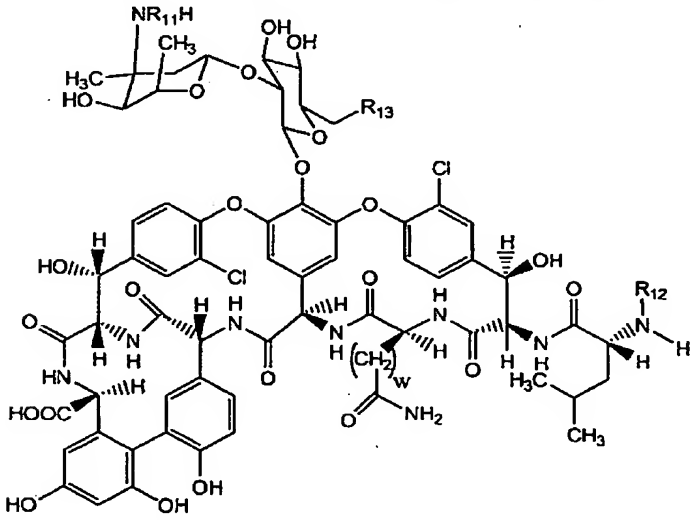
13. (Original) The method of claim 10, wherein said solvent mixture comprises about equal parts dichloromethane and dichloroformamide.

14. (Original) The product prepared by the method of claim 1.

15. (Original) The product prepared by the method of claim 10.

16. (Original) The method of claim 1, wherein said molar excess of triethylamine is at least about 30-fold.

17. (Original) A method of preparing a vancomycin-polymer conjugate wherein said conjugate has a polymer residue attached on both the sugar amino and the N-methyl amino of said vancomycin compound, comprising: reacting a vancomycin compound of the formula:



wherein

R_{11} and R_{12} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} hetero-alkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxyalkyl, phenoxyalkyl, and C_{1-6} heteroalkoxys;

R_{13} is OH, NH-aryl, NH-aralkyls, NH-alkyl-aryl or NH-C_{1-12} alkyl; and

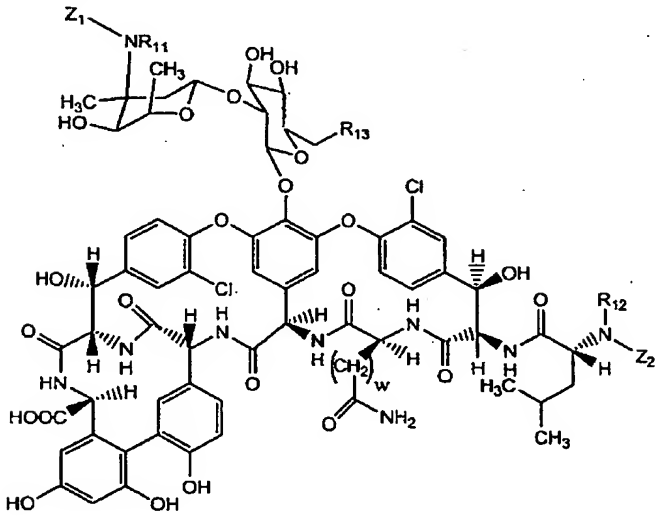
w is 1 or 2;

with at least about 2 equivalents of a polymer residue containing at least one leaving group capable of reacting with the sugar amino group and the N-methyl amino group of said vancomycin compound in the presence of at least about a five-fold molar excess of dimethylaminopyridine (DMAP) and a sufficient amount of a solvent mixture comprising dichloromethane (DCM) and dimethyl formamide (DMF).

18. (Original) The method of claim 17, wherein said solvent mixture comprises about equal parts dichloromethane and dichloroformamide.

19. (Original) The product prepared by the method of claim 17.

20. (Currently Amended) The product prepared by the method of claim 19, wherein said vancomycin-polymer conjugate comprises the formula:



wherein:

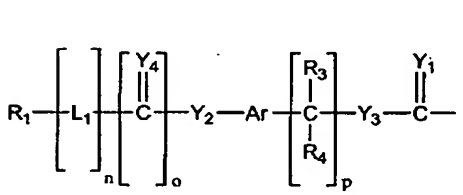
R_{11} and R_{12} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxyalkyl,

phenoxyalkyl and C_{1-6} heteroalkoxys;

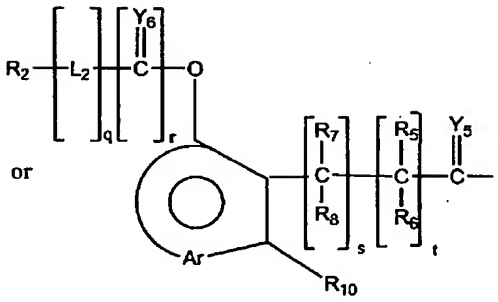
R_{13} is OH, NH-aryl, NH-aralkyls, or NH-C_{1-12} alkyl; and

w is 1 or 2;

Z_1 and Z_2 are



or



wherein

R_1 and R_2 are independently selected polymeric residues;

Y_{1-6} are independently selected from the group consisting of O, S or NR_9;

R_{3-10} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cyloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxy, phenoxy and C_{1-6} heteroalkoxy;

Ar is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

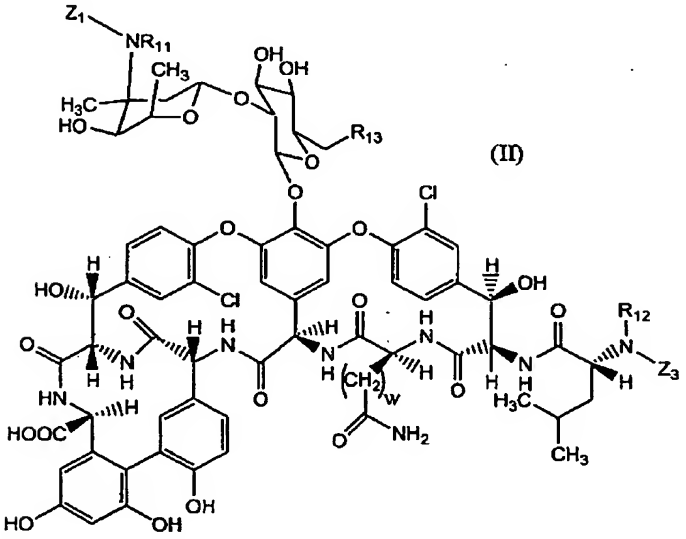
L_1 and L_2 are independently selected bifunctional linkers;

p and t are independently selected positive integers;

n, q and s are independently either zero or a positive integer; and

o and r are independently zero or one.

21. (Original) A vancomycin polymer conjugate comprising the formula:



(II)

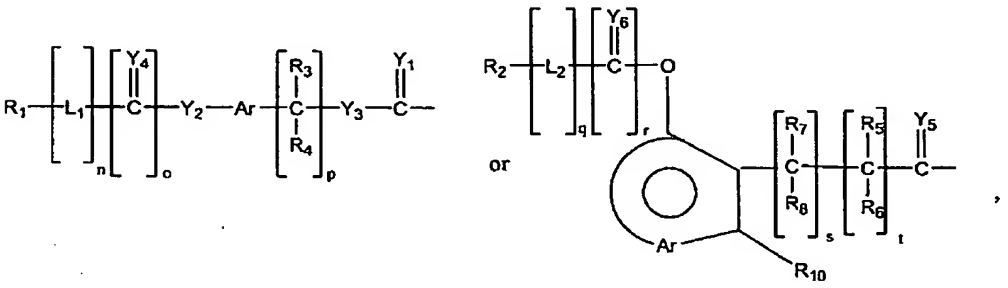
wherein:

R_{11} and R_{12} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxyalkyl, phenoxyalkyl, and C_{1-6} heteroalkoxys;

R_{13} is OH, NH-aryl, NH-aralkyls, or NH-C_{1-12} alkyl;

w is 1 or 2; and

Z_1 is



wherein

R_1 and R_2 are independently selected polymeric residues;

Y_{1-6} are independently selected from the group consisting of O, S or NR_9;

$R_{3\text{-}10}$ are the same or different and are each independently selected from the group consisting of hydrogen, $C_{1\text{-}6}$ alkyls, $C_{3\text{-}12}$ branched alkyls, $C_{3\text{-}8}$ cycloalkyls, $C_{1\text{-}6}$ substituted alkyls, $C_{3\text{-}8}$ substituted cyloalkyls, aryls, substituted aryls, aralkyls, $C_{1\text{-}6}$ heteroalkyls, substituted $C_{1\text{-}6}$ heteroalkyls, $C_{1\text{-}6}$ alkoxys, phenoxys and $C_{1\text{-}6}$ heteroalkoxys;

Ar is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

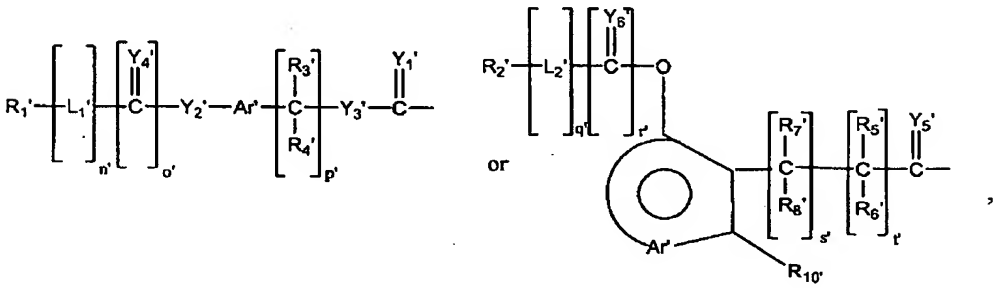
L_1 and L_2 are independently selected bifunctional linkers;

p and t are independently selected positive integers;

n, q and s are independently either zero or a positive integer; and

o and r are independently zero or one; and

Z_3 is



wherein

R_1' and R_2' are independently selected polymeric residues;

$Y_{1\text{-}6}'$ are independently selected from the group consisting of O, S or NR_9';

$R_{3\text{-}10}'$ are the same or different and are each independently selected from the group consisting of hydrogen, $C_{1\text{-}6}$ alkyls, $C_{3\text{-}12}$ branched alkyls, $C_{3\text{-}8}$ cycloalkyls, $C_{1\text{-}6}$ substituted alkyls, $C_{3\text{-}8}$ substituted cyloalkyls, aryls, substituted aryls, aralkyls, $C_{1\text{-}6}$ heteroalkyls, substituted $C_{1\text{-}6}$ heteroalkyls, $C_{1\text{-}6}$ alkoxy, phenoxy and $C_{1\text{-}6}$ heteroalkoxy;

Ar' is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

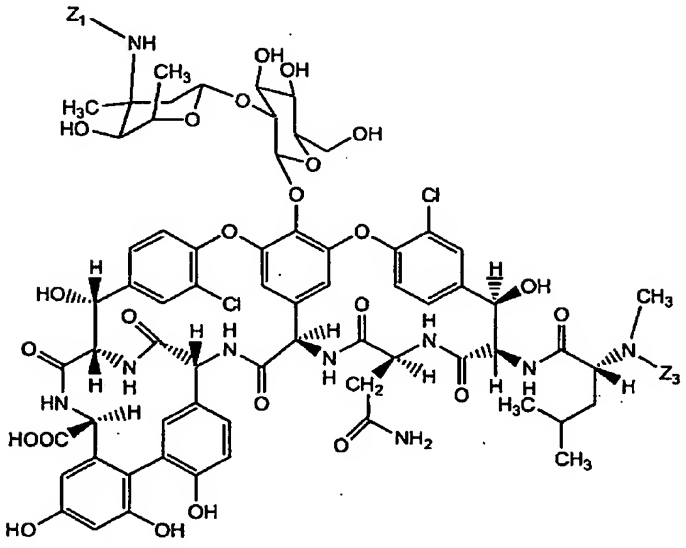
L_1' and L_2' are independently selected bifunctional linkers;

p' and t' are independently selected positive integers;

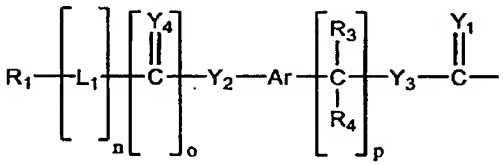
n', q' and s' are independently either zero or a positive integer; and

o' and r' are independently zero or one.

22. (Original) A vancomycin polymer conjugate of claim 21, comprising the formula

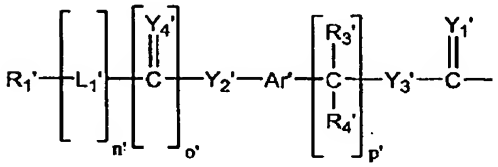


23. (Original) The vancomycin polymer conjugate of claim 22, wherein Z_1 is

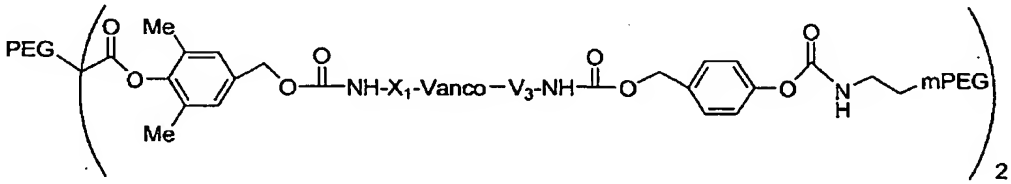


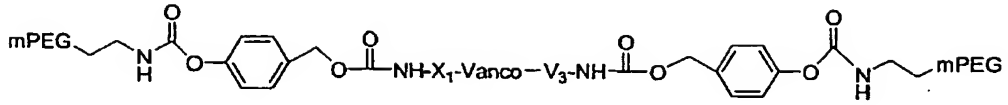
and

Z_3 is

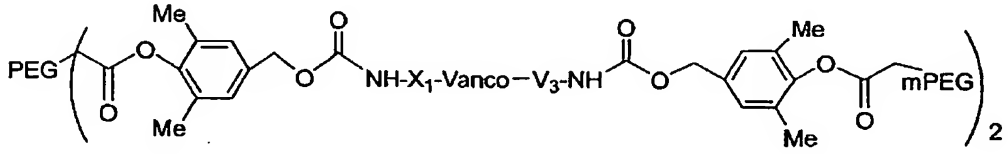


24. (Original) A vancomycin polymer conjugate of claim 21, selected from the group consisting of:





and



25. (Original) The polymer conjugate of claim 21, wherein Y_{1-4} and Y_{1-4}' are each O.

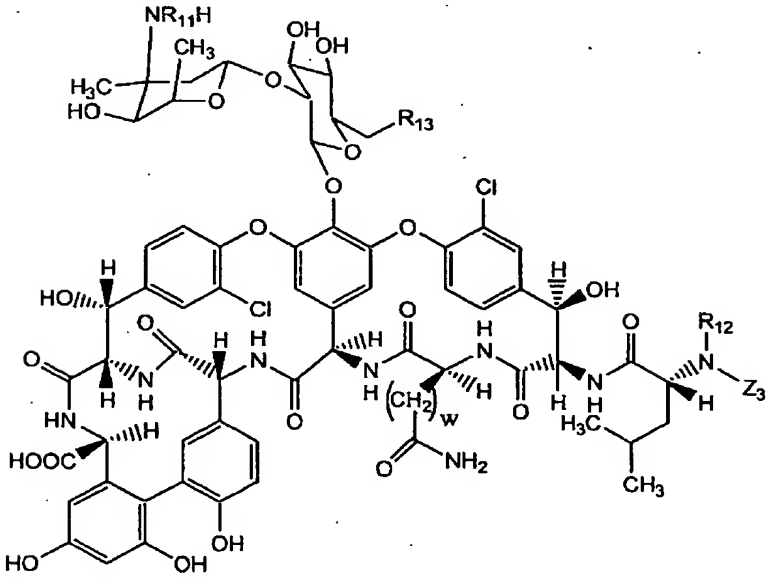
26. (Original) The polymer conjugate of claim 21, wherein R_{3-8} and R_{3-8}' are independently selected from the group consisting of hydrogen, methyl and ethyl; and p, p', t and t' are each one.

27. (Original) The polymer conjugate of claim 21, wherein R_1, R_1', R_2 and R_2' are independently selected polyalkylene oxide residues.

28. (Original) The polymer conjugate of claim 21, wherein R_1, R_1', R_2 and R_2' are independently selected polyethylene glycol residues.

29. (Original) The polymer conjugate of claim 27, wherein said polyalkylene oxide has a weight average molecular weight of from about 2,000 Da to about 100,000 Da.

30. (Original) A vancomycin-polymer conjugate comprising the formula:



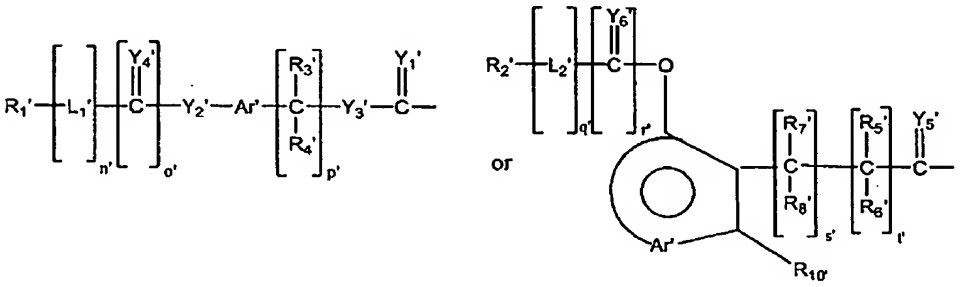
wherein

R_{11} and R_{12} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxyalkyl, phenoxyalkyl, and C_{1-6} heteroalkoxys;

R_{13} is OH, NH-aryl, NH-aralkyl, or NH-C_{1-12} alkyl; and

w is 1 or 2;

Z_3 is



wherein

R_1' and R_2' are independently selected polymeric residues;

Y_{1-6}' are independently selected from the group consisting of O, S or NR_9';

R_{3-10}' are the same or different and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxys, phenoxys and C_{1-6} heteroalkoxys;

Ar' is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

L_1' and L_2' are independently selected bifunctional linkers;

p' and t' are independently selected positive integers;

n', q' and s' are independently either zero or a positive integer; and

o' and r' are independently zero or one.

31. (Original) A method of treatment, comprising administering an effective amount of a compound of claim 21.

32. (Currently Amended) A method of treating a vancomycin susceptible disease in a mammal comprising administering an effective amount of a compound of claim 10 ~~1~~, to a mammal in need of such treatment, whereby, the compound of claim 10 ~~1~~ undergoes degradation and releases vancomycin or a vancomycin derivative *in vivo*.

33. (Original) A method of treating a vancomycin susceptible disease in a mammal comprising administering an effective amount of a compound of claim 21, to a mammal in need of such treatment, whereby, the compound of claim 21 undergoes degradation and releases vancomycin or a vancomycin derivative *in vivo*.

34. (Currently Amended) A method of treating a vancomycin susceptible disease in a mammal comprising administering to a mammal in need of such treatment, an effective amount of a combination of vancomycin or a pharmaceutically acceptable salt, solvate or hydrate thereof, and a compound of claim 10 ~~1~~, wherein said vancomycin and said compound of claim 10 ~~1~~ are administered either substantially concurrently in separate dosage forms or combined in a unit dosage form.

35. (Currently Amended) A kit comprising in separate containers in a single package, pharmaceutical compositions for use in combination to treat a vancomycin susceptible disease which comprises in one container a therapeutically effective amount of vancomycin or a pharmaceutically acceptable salt, solvate or hydrate thereof in a pharmaceutically acceptable carrier and in a second container a therapeutically effective amount of a compound of claim 10 ~~1~~ or a pharmaceutically acceptable salt, solvate or hydrate thereof in a pharmaceutically acceptable carrier.